

### **REMARKS/ARGUMENTS**

#### **The Double Patenting Rejection**

In the a previous Office Action the Examiner rejected claims 1-32 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent 6,589,985.

Applicants argued that while a movement disorder might result from damage to the nervous system leading to cell death, this is not a necessary part of a movement disorder. Applicants urged that neurodegenerative disorders by definition involve the death or damage to the cells of the nervous system.

In the Office Action mailed on January 12, 2006 the Examiner stated that the Applicants' arguments were not persuasive and the rejection of record under the judicially created doctrine of obviousness-type double patenting was maintained. The Examiner stated that "By Applicants' own admission, i.e., "neurodegenerative disorders by definition involve the death or damage to the cells of the nervous system", those disorders recited in claims 20-22 of the patent involve death or damage to cells of the nervous system".

The Applicants respectfully disagree with the maintenance of this rejection for the following reason, Applicants contend that movement disorders and neurodegenerative disorders are fundamentally separate pathologic medical entities. It is true that some neurodegenerative disorders can cause some types of movement disorders for example Parkinson's Disease (a neurodegenerative disorder) can cause some types of movement disorder such as bradykinesia, rigidity, shuffling, gait, and cogwheeling but these same movement disorder symptoms can be produced in a normal person by neuroleptic drugs such as haloperidol. However, most movement disorders are not the result of neurodegenerative

disorders, for example, essential tremor, restless leg syndrome, tardive dyskinesia and most forms of tic disorders.

Medical textbooks classify most movement disorders under "extra pyramidal disorders" and most neurodegenerative disorders under "degenerative diseases of the nervous system" (see Cecil Textbook of Medicine 21<sup>st</sup> Edition, Goldman L. and Bennett J.C. editors, W.B. Saunders Co. Philadelphia (2000) Chapter 459 p 2077 and Chapter 465 p 2087).

Further, movement disorders and neurodegenerative disorders differ markedly in terms of treatment. For example beta-blockers are effective for the treatment of essential tremor but are of no value in the treatment of any type of neurodegenerative disorders. For the most part there are no approved effective treatments for the actual pathology of neurodegenerative disorders, that is there no treatments that can stop or slow the loss of neurons.

It is true that a number of movement disorders such as some of those in claims 20-22 of U.S. Patent 6,589,985 are the result of neurodegenerative disorders such as Parkinson's Disease or Huntington's Disease as the Examiner points out. However in the '985 patent the efficacy of the compounds of the invention is in treating the abnormal movement resulting from the underlying disorder, for example tremor in Parkinson's Disease or chorea in Huntington's Disease. By contrast, it is the intention of the present invention to provide compounds and treatment methods that slow or prevent the death or loss of neurons that represent the pathologic process underlying the neurodegenerative disorder itself.

Therefore Applicants respectfully request the withdrawal of the double patenting rejection.

The Rejections Under 35 USC 112 First Paragraph

The Examiner has maintained the rejection of claims 1-32 under 35 USC 112 first paragraph made in the previous Office Action.

The Applicants respectfully disagree with the maintenance of this rejection.

As the Applicants stated in the previous amendment, as the specification clearly states, both acute and chronic neurodegenerative disorders are associated with neuronal cell death or compromise. There are many clinical and diagnostic entities with various etiologies that are considered to be neurodegenerative disorders but they all result in the death or the serious compromise of the function of nerve cells. The final common pathways by which this death or neuronal dysfunction is produced is much less varied than the clinical diversity of neurodegenerative conditions would suggest. The biological experimental examples described in the specification demonstrate the efficacy of the compounds of the invention in preventing several of these final common pathways from causing cell death.

In Example 1 it was demonstrated that an enantiomer of the invention was able to prevent the activation of apoptotic mechanisms following serum withdrawal in an *in vitro* neuronal cell model. The apoptotic mechanisms involved in this model are characteristic of the causes of neuronal loss in many diverse neurodegenerative disorders. Therefore this model may be considered valid for a wide variety of neurodegenerative and cell death related disorders.

In Example 2 the enantiomers of the invention were shown to reduce the volumes of neuronal injury or infarction in rat brains after transient cerebral ischemia due to mild cerebral artery occlusion. Ischemia is the most general and non-specific possible stress for

neurons as it produces a deprivation of both oxygen and nutrients and provokes both apoptotic and necrotic cell loss mechanisms. Thus, reduction of neuronal cell death in this model would imply efficacy of the genus of compounds of the invention in a wide variety of neurodegenerative disorders and in stroke and many other related pathological states.

Applicants submit that the experimental results submitted demonstrate the effectiveness of the compounds encompassed in the entire genus of compounds disclosed to suppress the final common pathways of apoptotic and ischemic cell death mechanisms characteristic of the wide variety of neurodegenerative disorders as claimed.

The Examiner contends that these examples are **prophetic**, apparently because of the use of the phrase "would imply" in the Applicants' previous amendment. Applicants wish to respectfully point out that the past tense is consistently and properly used in the descriptions of both examples 1&2 themselves in the specification. The examples in the specification are definitely **not** prophetic but were actually performed. The use of the phrase "would imply" in my previous amendment referred only to the belief that such established experimental results would imply that the compounds of the invention would be effective in treating or preventing neurodegeneration disorder in humans in clinical trials.

Therefore the Applicants respectfully request the withdrawal of the rejection of claims 1-32 under 35 USC 112 first paragraph.

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Response to Office Action dated January 12, 2006

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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